claimed invention. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379 (Fed. Cir. 1986).

As discussed above, Claim 1 has been cancelled without prejudice to future prosecution, and new Claim 72 has been added. Respectfully, Applicants assert that Martins fails to expressly teach each and every element of new Claim 72.

New Claim 72 relates to a method of obtaining a sustained CTL response in a mammal. The method includes delivering an antigen directly to the lymphatic system of the mammal at a level sufficient to induce a CTL response in the mammal, maintaining the antigen in the mammal's lymphatic system sufficient to maintain the CTL response for a period of time that is substantially co-extensive with the desired duration of the CTL response, obtaining a sustained CTL response in the mammal, and detecting the sustained CTL response in the mammal.

Martins clearly does not teach, directly or inherently, each and every element of new Claim 72. As non-exclusive examples, first, as pointed out in the Final Office Action, Martins fails to disclose delivering an antigen directly to the lymphatic system of the mammal. Second, Martins fails to maintain the antigen in the mammal's lymphatic system sufficient to maintain the CTL response for a period of time that is substantially co-extensive with a desired duration of the CTL response.

Third, Martins fails to disclose obtaining a sustained CTL response. Fourth, Martins does not disclose detecting a sustained cytotoxic T lymphocyte (CTL) response in the mammal. Martins reports obtaining and detecting antibody responses. *See* Martins at Examples 1-4; specifically, column 8, lines 48-51; column 9, lines 56-63; column 10, lines 65-68; and column 14, lines 33-35. Also, Martins reports testing for allergic reactions by detecting delayed type hypersensitivity (DTH). *See id.* at Example 4. However, detecting antibody or DTH is not the same as detecting a sustained cytotoxic T cell response. In sum, Martins does not obtain or detect a sustained CTL response.

For all of the above reasons, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 102, and allowance of the pending claims.

Discussi n of Rejection Under 35 U.S.C. § 103

The Office Action rejected Claims 2, 3, 5-6, 11-13, 15-16, and 20-21 under 35 U.S.C. § 103(a) as being unpatentable over Martins as applied to Claims 1 and 4 under § 102(b) above

in view of Kundig (*Science*, 268:1343-1347). Claims 17-19, 41-42, and 53-54 were rejected under § 103(a) as being unpatentable over Martins, as applied above to Claims 4, 39 and 48 under § 102(b), and further in view of Falo, Jr., et al. ("Falo Jr.") (U.S. Patent No. 5,951,975). Further, the Office Action rejected Claims 40 and 60 under § 103(a) as being unpatentable over Martins as applied to Claims 39 and 59 above under § 102(b), and further in view of Eberlein et al. ("Eberlein") (U.S. Patent No. 5,550,214).

To establish a *prima facie* case of obviousness, a three-prong test must be met. First, there must be some suggestion or motivation, either in the references or in the knowledge generally available among those of ordinary skill in the art, to modify the primary reference. Second, there must be a reasonable expectation of success found in the prior art. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). Third, the prior art reference must teach or suggest all the claim limitations. *See* M.P.E.P. §2143; *In re Royka*, 490 F.2d 981 (CCPA 1974).

As discussed above, Martins fails to teach each and every element of the claims. Martins, even in view of the other cited references, fails to teach or suggest all of the features of the claims.

New Claim 72 is not obvious over Martins when combined with Kundig because the references, even if combined, still do not disclose each and every element of new Claim 72. Kundig reported that a fibroblast can serve as an antigen presenting cell (APC), thus leading to immunization, if the fibroblast reaches a lymphoid environment. *See Kundig* at pages 1343, 1345. An APC is a type of cell which provokes an immune response from T lymphocytes by presenting antigenic fragments at its surface and then interacting with the T lymphocytes. Kundig showed that the route of injection determines the efficiency of this type of immunization. *See Kundig* at pages 1344-1345. Subcutaneous (s.c.), intraperitoneal (i.p.), and intrasplenic (i.spl.) injections require progressively smaller doses. *See id.*

However, Kundig does not teach maintaining the antigen in the mammal's lymphatic system sufficient to maintain the CTL response for a period of time that is substantially co-extensive with a desired duration of the CTL response. Also, Kundig does not disclose obtaining a sustained CTL response. Furthermore, Kundig does not disclose detecting a sustained CTL response. Thus, Martins in view of Kundig still fails to render the present invention obvious. Falo Jr. and Eberlein do not disclose the features of the claims lacked by Martins and/or Kundig.

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Therefore, for the reasons set forth above, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. §103.

CONCLUSION

Applicants have endeavored to address all of the Examiner's concerns as expressed in the outstanding Final Office Action. Accordingly, amendments to the claims, the reasons therefor, and arguments in support of the patentability of the pending claim set are presented above. In light of the above amendments and remarks, reconsideration and withdrawal of the outstanding rejections is specifically requested. If the Examiner finds any remaining impediment to the prompt allowance of these claims that could be clarified with a telephone conference, the Examiner is respectfully requested to initiate the same with the undersigned.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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Dated: 9/18/02

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Please amend Claims 3, 4, 39, 44, 48, 50, 51, 61, 62, 66, and 67 as follows:

3. (Amended) The method of Claim [2]72, wherein the CTL response is maintained by delivering the antigen directly to the spleen, a lymph node or lymph vessel.

4. (Thrice Amended) The method of Claim [1]72, wherein the antigen is a disease matched antigen.

39. (Amended) The method of claim [1]72, wherein said antigen is provided as a polypeptide.

44. (Amended) The method of claim [1]72, wherein said antigen is provided as a component of a microorganism.

48. (Twice Amended) The method of claim [1]72, wherein said antigen is provided as a nucleic acid encoding the antigen.

50. (Twice Amended) The method of claim [1]72, wherein said antigen is provided as a vector comprising a bacterium.

51. (Twice Amended) The method of claim [1]72, wherein said antigen is provided as a vector comprising a virus.

61. (Amended) The method of Claim [1]72, wherein the antigen is delivered as a bolus in a single dose, and wherein the singe dose is sufficient to maintain the immunologic CTL response.

62. (Amended) The method of Claim [1]72, wherein the antigen is maintained by sustained, regular delivery of the antigen.

66. (Amended) The method of claim [1]72, wherein said sustained exposure of the antigen to the mammal's lymphatic system comprises continuous exposure of the antigen to the mammal's lymphatic system.

67. (Amended) The method of claim [1]72, wherein said sustained exposure of the antigen to the mammal's lymphatic system comprises repeated exposure of the antigen to the mammal's lymphatic system.